

### **REMARKS**

Claims 1-74 were pending prior to this Response, with claims 67-69 having been withdrawn from further consideration pursuant to 37 C.F.R. §1.142(b), and claims 71, 72 and 74 having been deemed allowable. Further, claims 41-47, 51, 62, 63 and 70 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

By the present communication, no claims have been added or canceled, and claims 30 and 35-38 have been amended to recite Applicants' invention with greater particularity. Support for the amendments can be found throughout the application as filed. In particular, support for the amendment to claim 30 can be found, for example, at paragraph 0040. Support for the amendments to claims 35-38 can be found, for example, in the claims as originally filed and at, for example, paragraphs 0033, 0047 and 0049. Applicant respectfully requests entry of the amendments set forth in this response under 37 CFR §1.116. The amendments do not raise any issues of new matter and the amended claims do not present new issues requiring further consideration or search. Accordingly, claims 1-66 and 70-74 are currently pending in this application.

Applicants have reviewed the rejections set forth in the Office Action mailed June 30, 2005, and respectfully traverse all grounds for the reasons that follow.

### **Objections to the Specification**

The specification is objected to under 37 C.F.R. §1.75(d)(1) for allegedly failing to provide proper antecedent basis for the subject matter of claims 12-13 and 46-47, directed to a computer readable medium or media, or to a method, where a biochemical reaction network represents reactions occurring in a first cell and a regulatory data structure represents events occurring in a second cell of a population of cells. The population of cells can be a multicellular organism. The Office Action alleges that none of paragraphs [0033], [0038], [0135] and [0136], individually or collectively describe the concept of claims 12-13 and 46-47.

Applicants submit that the cited paragraphs provide sufficient antecedent basis for the claimed invention. The claims are directed to a biochemical reaction network and a regulatory data structure occurring in different cell populations and the cited paragraphs pointed out in Applicants' previous response provide the requisite basis. These teachings are further delineated below.

Paragraph [0033] teaches that that a regulatory data structure refers to first and second reactions related by an altered flux.

Paragraph [0038] teaches that a biochemical reaction network of the claimed invention can be represented by a data structure relating reactants and reactions. The reactants can be assigned to different compartments. Examples of compartments include the intracellular space of a cell. Therefore, if reactants are in two different compartments they reside in different cells.

Paragraph [0136] teaches use of the methods of the invention to model events occurring in different cells of an organism when it describes that the methods can be used to a simulate signal transduction and physiological systems. Both of these examples describe a biochemical reaction network representing reactions occurring in a first cell and a regulatory data structure representing events occurring in a second cell of a multicellular organism.

Accordingly, the above paragraphs teach a regulatory data structure where one reaction alters the flux of another reaction and that data structures and biochemical networks can occur in different compartments or cells. These teachings and exemplifications provide sufficient antecedent basis for claiming a medium, media or method where a biochemical reaction network represents reactions occurring in a first cell and a regulatory data structure represents events occurring in a second cell of a population of cells.

Further, paragraph [0135] provides sufficient antecedent basis for the dependent claims because it teaches that the invention can be used to model a variety of organisms, including eukaryotic organisms and the multicellular human organism.

Therefore, Applicants maintain that the application provides sufficient antecedent basis for claims 12-13 and 46-47 and respectfully request that this ground of objection be withdrawn.

**Rejections under 35 U.S.C. §101**

Claims 1-20 and 23-33 stand rejected under 35 U.S.C. §101 for being directed to non-statutory subject matter as allegedly nonfunctional descriptive material. Appearing to acknowledge that the data structure contained on the claimed computer readable medium or media is employed as a computer component, the Office nevertheless alleges that the functionality of the data structure is not claimed irrespective of the claimed relationships. In particular, the Office alleges that the claim does not require the data structure and the constraint set of the claimed computer readable medium or media to interact with a computer in execution of any method. The Office cites to *In re Lowry* as support for alleging that the claims require an element requiring functional interaction with a computer.

Applicants submit that reliance on *In re Lowry* for requiring a functional interaction with a computer is inapplicable to the claimed invention. As pointed out in Applicants' previous response, it is the M.P.E.P. that cites to *In re Lowry* as an example of a statutory patentable data structure. The Federal Circuit decision simply points out that the Board overturned the PTO's §101 rejection, holding that the claims, directed to a memory containing stored information recited an article of manufacture and was statutory subject matter. *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994). The Court provided no indication that the Office's apparent requirement for a functional interaction with a computer was necessary or considered for deciding the statutory subject matter question. Rather, the functional relationship of the claimed data structure with a computer was addressed as a prior art rejection under §103. Therefore, any discussion of a functional relationship and reliance on *In re Lowry* is inapplicable to the rejection addressed here under §101. Moreover, even in addressing the prior art rejection, the Court made no determination that a functional relationship between a data structure and a computer required a "specific recitation" that the data structure be "executed" or "used" by the computer as asserted by the Office.

Further, The Board of Appeals and Interferences of the U.S. Patent and Trademark Office has recently overturned rejections attempting to require method claims to include machine or computer processing limitations such as the instant requirement for interaction with a computer. *In re Lundgren*, B.P.A.I. Case Nos. 2003-2088 (Sept. 28, 2005) (*Per Curium*). This decision by the U.S.P.T.O. itself establishes a new precedent invalidating Examiners' rejections which allege nonstatutory subject matter because the claims lack a relationship to the "technological arts" when they do not require machine implementation. In light of *In re Lundgren*, withdrawal of this ground of rejection is respectfully requested.

### **Rejections Under 35 U.S.C. § 112**

Applicants acknowledge that the rejection of claims 1-33 under 35 U.S.C. § 112, second paragraph, as allegedly unclear has been withdrawn and that the Office interprets the claims to include, for example, a data structure and constraint set on different media or multiple copies on the same media. However, the Office considers the claims to not include interactions between a data structure and a constraint set and relies on the reasons set forth under the §101 rejection above.

Applicants submit that the reasons for rejecting the claims under §101 above fail to explain why the claims are allegedly unclear. Whether the claims are definite is a separate inquiry from whether they fall under statutory subject matter.

Further, claims 1-33 are clear and expressly recite an interaction between the data structure and the constraint set. In particular, claim 1, step (a) recites a data structure relating a plurality of reactants to a plurality of reactions. Therefore, step (a) claims a relationship between reactants and reactions. Step (b) recites a constraint set for the plurality of reactions. Therefore, step (b) claims a constraint set that serves or is placed on the plurality of reactions. As set forth in the definition of the term, a "constraint" places an upper or lower boundary on a reaction. Therefore, the constraint set places boundaries on the plurality of reactions. In light of this plain language of the claims, Applicants respectfully disagree with the Office's interpretation that there is no interaction between the claimed data structure and constraint set because there is a clearly claimed relationship between these two elements.

Claims 2-7, 9-13, 26-30 and 32-33 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because they fail to further limit their respective base claims. The Office asserts that Applicants response failed to explain or clarify how the scope of the claims differ and construes Applicants statement with respect to whether the dependent claims alter the structure of the claimed data structure to whether the dependent claims alter the scope of the claimed data structure, concluding that any failure to alter the structure also fails to further limit the scope of the dependent claims.

Applicants respectfully submit that such a general analogy is inappropriate. Altering the scope of a dependent claim compared to its base claim does not require altering the structure of one of the claimed elements. A data structure is “a physical or logical relationship among data elements, designed to support specific data manipulation functions.” *The New IEEE Standard Dictionary of Electrical and Electronics Terms* 308 (5th ed. 1993). Altering a characteristic of one of the related elements of the data structure alters the claimed relationship between the plurality of reactant and the plurality of reactions. Therefore, in the example provided by the Office, changing the reactant from insulin to nerve growth factor changes the claimed relationship between the plurality of reactants and the plurality of reactions. Accordingly, Applicants submit that the dependent claims are clear and properly further limit their base claims because the claimed relationships are changed. Withdrawal of this ground of rejection is respectfully requested.

Claim 14 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because the term “constraint function” is confusing as to whether it refers to an equation, data, executable instruction or command. The Office alleges that Applicants’ reference to paragraph 0074 and Figure 3 fail to limit the definition of the term with respect to the claims and that Figure 3 illustrates a model or process rather than what was intended to be present on a computer readable medium

The requirement for precision in claiming is set forth in the second paragraph of § 112. The statute is satisfied if a person skilled in the field of the invention would reasonably understand the claim when read in the context of the specification. *Marley Moldings Limited v. Mikron Industries, Inc.*, Case No.04-1441, slip op. at 5 (Fed. Cir. August 8, 2005) citing *Union Pac. Res. Co. v. Chesapeake Energy Corp.*, 236 F.3d 684, 692 (Fed. Cir. 2001) (the definiteness

requirement of §112, second paragraph “focuses on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the rest of the specification”). The term “constraint function” when read in light of the specification reasonably apprises those skilled in the art of the scope of the claim.

Although the Office points to paragraph 0074 and Figure 3 referenced in Applicants’ previous response, also included therein were specific references to paragraphs 0048 and 0049. In particular, the meaning of the terms “constraint” and “function” are defined therein. A constraint refers to an upper or lower boundary for a reaction in the claimed data structure and constraint. The term “function” is accorded its ordinary meaning in the computer and mathematical arts. The meaning of this term is exemplified as a logic statement at, for example, paragraph 0074 and in Figure 3. Therefore, when read in light of the specification, one skilled in the art would understand the term “constraint function” to mean a logic statement or other computer or mathematical statement that assigns one element of one set to an element of the same or another set and which has an upper or lower boundary. The definiteness of this term, as outlined above and throughout the application as filed, is sufficiently precise to satisfy the requirements of §112, second paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Claim 30 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly for use of the term “confidence rating.” The Office alleges that the claim fails to require that the rating is with respect to the belief that a reaction occurs in a particular biochemical reaction network and that Applicants’ reference to paragraph 0040 is an improper reading of a limitation into the claim. merely states that it is unclear what this term references.

As set forth above, the requirements of § 112, second paragraph, are satisfied if one skilled in the art would reasonably understand the meaning of the claim when read in context of the specification. *Marley Moldings Limited*, Case No.04-1441, slip op. at 5. As set forth in paragraph 0040, for example, the computer readable medium or media can contain an annotation that includes “a level of confidence with which a reaction is believed to occur in a particular biochemical reaction network or organism.” In light of this description, one skilled in the art would reasonably understand that the term refers to a level of confidence for a reaction to occur. Nevertheless, to further prosecution of this application, Applicants have amended claim 30 to

recite this language from the specification. In light of this amendment, this ground of rejection is moot and its withdrawal is respectfully requested.

Claims 35-39 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because it is unclear whether this claim recites an active step to update a value in the constraint set.

As pointed out in Applicants' previous response, independent claim 34 recites providing a condition-dependent value to the claimed variable constraint. Claims 35-39 further specify the origin of the condition-dependent value. A depend claim can properly limit its base claim by further characterizing an element or step of the composition or method. Although the claims are clear as written, Applicants have amended these claims to clearly specify the condition to which the condition-dependent value is conditioned upon. In light of these amendments, this ground of rejection is moot and Applicant respectfully requests its withdrawal.

Claims 48-50 and 52 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite allegedly because further recitation of a constraint function fails to set forth an additional step or modify an existing step. The Office alleges that these claims appear to be directed to a method with a constraint function capability and that it is unclear whether or not that capability is used.

As previously pointed out, a constraint function refers to a logic statement or other computer or mathematical statement that assigns one element of one set to an element of the same or another set and which has an upper or lower boundary. In light of this meaning, as one skilled in the art would understand it when read in context of the entire specification, the term is sufficiently clear to describe how the data structure is used in the method of claim 48 when it additionally contains a constraint function. Therefore, withdrawal of this ground of rejection is respectfully requested.

Claim 55 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite for use of the term "modifying" allegedly because the claim is unclear as to what is modified, how it is modified or why it is modified. The Office asserts that the claim is not limited to a format manipulation such as the changes referenced in paragraphs 0032-0033 and 0047-0048 and that it is not clear what aspect of the constraint set or data structure is intended to be modified.

Applicants submit that claim 55 is clear and definite. To satisfy § 112, second paragraph, Applicant is only required to particularly claim the invention such that one skilled in the art would reasonably understand the meaning of the claim when read in context of the specification. *Marley Moldings Limited*, Case No. 04-1441, slip op. at 5. The application describes at, for example, paragraph 0037 that a data structure corresponds to a representation of information in a format that can be manipulated. Therefore, the claimed relationship of the plurality of reactants and reactions of the data structure wherein one of the reactions is a regulated reaction can be modified by manipulation. Thus, the claim is sufficiently clear in light of the specification. It is the relationships of the data structure or, for example, the constraint set that can be modified. Regulatory reactions that can impart the modifications were set forth in Applicants' previous response and are exemplary. Thus, the application teaches and exemplifies modifications of a data structure or a constraint set that can be implemented using the methods of the invention and is clear as written and withdrawal of this ground of rejection is respectfully requested.

Claims 64-66 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because it is unclear how the claimed gene database modifies the method of base claim 34. The Office alleges that the claim does not contain a step to include the information from the gene database in the data structure and that the term "relating" refers to a description of what is present in the database rather than an action.

As pointed out previously, a dependent claim is proper if it further limits its base claim. There is no requirement for the dependent claim to perform an additional step. Claim 64 is directed to providing a gene database relating one or more reactions in the claimed data structure of base claim 34 with one or more open reading frames or proteins. Claim 64 adds the requirement of relating gene or protein information with the claimed data structure relationship of a plurality of reactants and reactions. The plain meaning of the term relating requires an interaction between the relationship information of the data structure and the information of the gene database because the term shows or establishes a connection between these two components. *See, e.g., Webster's Third New International Dictionary, Unabridged*. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> ("to show or establish a logical or causal connection"). The term "relating" does not solely describe what is present in the database. Rather, the term refers to providing a connective relationship between the information present in



both the data structure and in the database. Accordingly, the claims are sufficiently clear to satisfy the requirements of the second paragraph of § 112 and withdrawal of this ground of rejection is respectfully requested.

Claim 73 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite allegedly because the term “change in an environmental condition” is unclear. The Office alleges that the variable of claim 71 is not required to be related to an environmental condition.

Applicants submit that the claimed value can be based on a variety of conditions, including environmental conditions (see, for example, application at para. 0049 and Applicants’ previous response). Therefore, when read in context of the application, one skilled in the art would understand that the term “variable constraint” to include and, therefore, “relate” to an environmental condition. Further, Applicants respectfully point out that that claim 73 would be superfluous to claim 71 if the claimed variable constraint of claim 71 was required to be limited to an environmental condition. Accordingly, claim 73 is properly dependent on claim 71 and clear as written. Withdrawal of this ground of rejection is respectfully requested.

### **Priority**

The Office alleges that support for the claimed invention is not found in the priority applications. The Office simply concludes that the claimed computer readable medium or media or the methods of determining a systemic property are not disclosed in the priority applications and places the initial burden on Applicants to show such support.

Applicants submit that all claims are entitled to priority as of the earliest filed provisional application. Applicants respectfully submit that the Office has failed to provide an adequate showing or sufficient reasons why the instant claims are not supported in either or both of the provisional applications to which priority is claimed. It is up to the Office, in the first instance, to make a *prima facie* showing for lack of priority, and Applicant, in the second instance, to rebut the Office’s showing. Mere conclusory statements fail to provide a proper initial basis for asserting lack of priority and withdrawal of this ground of rejection is respectfully requested.

**Rejections Under 35 U.S.C. § 102**

Claims 1-3, 5-7, 17-20, 23-26, 29, 32-34, 40, 53-54, 56-61 and 64-66 stand rejected under 35 U.S.C. § 102(b) as anticipated by WO 00/46405 to Palsson. The Office asserts that WO 00/46405 describes regulated reactions and variable constraints allegedly because it describes limiting constraints on various fluxes, interpreting the constraints to be variable and the reactions they relate to regulated.

Claim 1 is directed to a computer readable medium or media having a data structure where at least one reaction is a regulated reaction and a constraint set having a variable constraint for the regulated reaction. Claim 34 is directed to a method for determining a systemic property of a biochemical reaction network which employs this data structure.

A finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). The Office must show that the single reference cited as anticipatory art describes all the elements of the claimed invention. The cited reference to WO 00/46405 fails to describe a variable constraint for regulated reaction as it is described and claimed in the subject application.

The invention claims a variable constraint, which is defined to mean that the value of the constraint is:

[C]apable of assuming any of a set of values in response to being acted upon by a function.

Application at para. 0049.

WO 00/46405 fails to describe a constraint being acted on by a function. WO 00/46405 also fails to describe that the constraints can assume any of a set of values when acted on by a function. Rather, the constraints referred to in WO 00/46405 are described as being set so as to provide limits to the linear equations (or linear programming equations) described therein. For example, Example 2, second paragraph describes the constraints as being “set.” Similarly, page 7, lines 19-27, describe the constraints as being “imposed” or “placed” on fluxes. Page 3, lines

15-36, describes that the constraints limited the fluxes, meaning that the activity of a flux is limited. No description in WO 00/46405 is apparent that describes a constraint being acted on by a function nor is there any description in WO 00/46405 of a constraint that is able to assume any of a set of values in response to function. Absent such a description of the claimed variable constraint, WO 00/46405 cannot anticipate the invention as claimed. Therefore, Applicants respectfully request withdrawal of this ground of rejection.

### **Rejections Under 35 U.S.C. § 103**

Claims 1-33 stand rejected under 35 U.S.C. § 103(a) as obvious over Edwards et al. The Office alleges that Edwards et al. describes a computer readable medium having a data structure and data, and that the data required by the claimed invention is considered to be non-functional descriptive material, which does not make an obvious invention patentable. The Office further alleges that Applicants' previous arguments with respect to Edwards et al. not teaching a method of determining a systemic property are not germane as no method claims have been rejected.

Applicants respectfully point out that the response previously filed with respect to this rejection was appropriately directed to the computer readable medium or media of claims 1-33. Applicants reassert their previous remarks and respectfully request the Office to fully consider them. Applicants previous remarks are quoted below for the Office's convenience and reconsideration.

To establish a *prima facie* case of obviousness, the Office must show that the prior art would have suggested the claimed invention to one of ordinary skill in the art and that it could have been carried out with a reasonable likelihood of success when viewed in the light of the prior art. *Brown & Williamson Tobacco v. Philip Morris*, 229 F.3d 1120, 1124 (Fed. Cir. 2000), accord *In re Royka*, 180 USPQ 580 (C.C.P.A. 1974) (to establish *prima facie* obviousness, all claim limitations must be taught or suggested by the prior art); M.P.E.P. §2143.03.

The alleged obvious rejection is based on the conclusion that the claimed relationships of the data structure and the claimed variable constraints correspond to non-functional descriptive material. However, and as described previously, the claimed data structure and variable constraints correspond to functional descriptive material because they consist of a physical or logical relationship among data elements which relate a plurality of reactants to a plurality of reactions of a biochemical network. Further, the claimed data structure and

variable constraints also impart functionality when employed as a computer component because they are used to determine a systemic property of a biochemical network. Therefore, the Office has failed to make a *prima facie* showing that Edwards et al. describes each and every element of the invention as claimed.

In particular, the Office neither provides a rational or points to particular descriptions in Edwards et al. that appear to show each element of the claimed computer readable medium or media or methods of determining a systemic property of a biochemical reaction network. For example, the Office has failed to show that Edwards et al. describe a computer readable medium or media or a method for determining a systemic property of a biochemical reaction network that includes a data structure relating a plurality of reactants to a plurality of reactions of a biochemical reaction network where at least one reaction is a regulated reaction and a constraint set having a variable constraint for the regulated reaction as claimed by the invention. Absent such a showing, the Office has not satisfied its burden. Because all the elements of the claimed invention are not taught or suggested in the cited reference, Edwards et al. cannot render the invention of claims 1-33 obvious and withdrawal of the rejection is respectfully requested.

In light of the above remarks, Applicants maintain that the claimed invention is unobvious over the cited art. Withdrawal of this ground of rejection is respectfully requested.

**CONCLUSION**

In summary, for the reasons set forth herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

A check in the amount of \$760.00 is enclosed, which includes 510.00 to cover a Three-Month Extension of Time fee, and \$250.00 to cover the Notice of Appeal fee. No additional fee is believed due in connection with this Response to the Final Office Action. In the event that any additional fee is due, the Commissioner is hereby authorized to charge any amounts required by this filing, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

Date: December 29, 2005



Lisa A. Haile, J.D., Ph.D.

Registration No. 38,347

Telephone: (858) 677-1456

Facsimile: (858) 677-1465

DLA PIPER RUDNICK GRAY CARY US LLP  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
**USPTO Customer Number 28213**